

**CERTIFICATE OF FILING**

I hereby certify that this paper and every paper referred to therein as being enclosed is being filed with the USPTO via facsimile to the designated fax number (571) 273-8300 or via EFS-Web and addressed to: Commissioner of Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on the date below

Date: September 28, 2009

By Jennifer Archer  
Jennifer Archer

Attorney Docket No. 100716-61  
Confirmation No. 4327

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

APPLICANT : Manfred T. REETZ et al  
SERIAL NO. : 10/530,818  
CUSTOMER NO. : 27384  
FILED : April 8, 2005  
FOR : MIXTURES OF CHIRAL MONOPHOSPHORUS COMPOUNDS  
USED AS LIGAND SYSTEMS FOR ASYMMETRIC TRANSITION  
METAL CATALYSIS  
ART UNIT : 1793  
EXAMINER : James E. McDonough

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

**DECLARATION UNDER 37 CFR § 1.132**

SIR:

I, Manfred T. Reetz, hereby declare as follows:

1. I am one of the inventors of the subject matter disclosed and claimed in U.S.

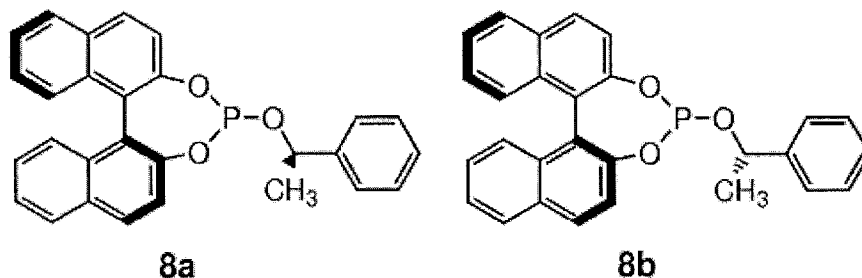
Patent Application Serial No. 10/530,818 (hereinafter "the present application").

2. My curriculum vitae is attached hereto as Exhibit 1.

3. In 1969, I was awarded the degree of Doctor of Philosophy from the Universität

Göttingen, Germany with U. Schöllkopf.

4. In 1993, I became Chairman of the Studiengesellschaft Kohle mbH.
5. I am an expert in biocatalysts, especially *in vitro* evolution of enantioselective and thermostable enzymes.
6. I have authored or co-authored over 470 publications; authored one book entitled "Organotitanium Reagents in Organic Synthesis;" and given over 125 plenary lectures and/or named lectures.
7. I have also been awarded over 20 United States patents, and a host of patents in other countries around the world.
8. I have been informed of the Office Action dated January 27, 2009, in the present application where the Examiner rejects the claims of the present application as being anticipated by or obvious over Reetz et al., *Angew. Chem. Int. Ed.*, 39: 3889-3890 (2000) (hereinafter "the Reetz article").
9. I co-authored the Reetz article.
10. In my opinion, the Reetz article does not anticipate or render obvious the subject matter of the claims of the present application.
11. The Reetz article describes two compounds 8a and 8b, which are described as diastereomeric ligands.
12. The structure of these two compounds 8a and 8b is as follows:



13. As I understand it, the claims of the present application all require “[a] chiral transition metal catalyst comprising at least two constitutionally different monophosphorus ligands bonded to a transition metal, at least one monophosphorus ligand being chiral.”

14. The compounds 8a and 8b in the Reetz article are not constitutionally different and, therefore, do not satisfy the terms of the claims of the present application.

15. I understand that excerpts from the well-known textbook, *Stereochemistry of Organic Compounds* by Ernest Eliel and Samuel Wilen, Wiley & Sons, Inc., New York, NY, 1994 (hereinafter “the Eliel text”), have been filed in the present application, and that these excerpts include explanations of the terms “constitution” and “configuration.”

16. “Constitution” refers to the number, kind and connectivity of the atoms in a molecule (see the third paragraph on page 15 of the Eliel text).

17. If two molecules have the same number of atoms, the same kind of atoms and the atoms all have the same connections, then the two molecules have the same “constitution.”

18. Molecules of the same “constitution” can differ in structure (see the first paragraph on page 18 of the Eliel text).

19. Two molecules that have the same constitution, but differ in structure are said to differ in “configuration.”

20. The two molecules 8a and 8b from the Reetz article have the same constitution because they have the same number of atoms, the same kinds of atoms and all of the atoms have the same connections.

21. The two molecules 8a and 8b, however, do differ in structure, as the CH<sub>3</sub> molecule in each case occupies a different spatial orientation—in compound 8a, the CH<sub>3</sub>

molecule occupies space above the plane of the page, whereas in compound 8b, the CH<sub>3</sub> molecule occupies space below the plane of the page.

22. Thus, the compounds 8a and 8b have the same constitution, but different configuration.

23. Therefore, the compounds 8a and 8b from the Reetz article do not anticipate the claims of the present application, which, again, require “[a] chiral transition metal catalyst comprising at least two *constitutionally different* monophosphorus ligands bonded to a transition metal, at least one monophosphorus ligand being chiral.”

24. Further, in my opinion, the Reetz article would not have rendered the subject matter of the present claims obvious to persons skilled in the art at the time the present invention was made.

25. There are data in the instant specification that show that the use of at least two constitutionally different monophosphorus ligands in many cases provides higher enantiomeric excess (“ee”) values than the use of either of the corresponding homocombinations of the identical monophosphorus ligands.

26. For example, referring to Table 1 on pages 17-18 of the present specification, Entry 1 shows that the homocombination (R)Ia/(R)Ia gave an ee of 91.8% and Entry 3 shows the homocombination (R)Ic/(R)Ic gave an ee of 92.0%.

27. In contrast, Entry 16 shows the heterocombination (R)Ia/(R)Ic gave an ee of 97.9%, better than either (R)Ia/(R)Ia or (R)Ic/(R)Ic.

28. Similarly, Entry 4 shows the homocombination (R)Id/(R)Id gave an ee of 93.3%.

29. In contrast, Entry 17 shows the heterocombination (R)Ia/(R)Id gave an ee of 97.8%, better than either (R)Ia/(R)Ia or (R)Id/(R)Id alone.

30. Likewise, Entry 18 shows the heterocombination (R)Ic/(R)Id gave an ee of 94.1%, better than either (R)Ic/(R)Ic or (R)Id/(R)Id alone.

31. Entry 25 shows the heterocombination (R)IIa/(R)IIb gave an ee of 84.6%, better than either (R)IIa/(R)IIa or (R)IIb/(R)IIb alone.

32. Entry 40 shows the heterocombination (R)Ic/(R)IIa gave an ee of 96.4%, better than either (R)Ic/(R)Ic or (R)IIa/(R)IIa alone.

33. Entry 42 shows the heterocombination (R)Id/(R)IIa gave an ee of 98.0%, better than either (R)Id/(R)Id or (R)IIa/(R)IIa alone.

34. Entry 44 shows the heterocombination (R)Id/(R)IIb gave an ee of 97.2%, better than either (R)Id/(R)Id or (R)IIb/(R)IIb alone.

35. Entry 45 shows the heterocombination (R)Ic/(R)IIb gave an ee of 95.6%, better than either (R)Ic/(R)Ic or (R)IIb/(R)IIb alone.

36. These improvements in ee employing heterocombinations, as opposed to homocombinations, are surprising and unexpected in my view.

37. Moreover, these improvements are of practical significance.

38. The higher ee values of the heterocombinations means that the use of catalysts containing such heterocombinations in enantioselective transition metal-catalyzed processes improves the selectivity of the processes and the yields of the desired products.

39. There is nothing in the Reetz article that teaches or suggests that the use of heterocombinations of monophosphorus ligands in such catalysts can lead to an improvement in their enantioselectivity.

40. Consequently, I believe that a person having ordinary skill in this art would find the present discovery, as supported by the data in the instant specification, to be surprising and unexpected and, therefore, objective evidence of nonobviousness (an inventive step).

41. I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and that the foregoing statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Dated August 28, 2009

By M. T. Reetz  
Dr. Manfred T. Reetz